The association of the presence of antitoxin in the blood with negative skin tests to small amounts of toxin, which seems fairly constant in older children, is somewhat more variable in infancy, and certain older infants may have negative skin tests, even to considerable amounts of toxin, without demonstrable antitoxin in the blood.

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Action of Formaldehyde Upon Physiologically Active, Histamine-like Substance Produced by Gas Bacillus.

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The phenomenon of contracture, induced in surviving sections of guinea pig intestine, suspended in Tyrode solution, by the addition of very small amounts of gas bacillus culture[1] suggests that the active substance, possibly substances, contains one or more free ethylamine groups, attached to an aromatic nucleus of the general type R :aromatic nucleus :ethylamine.

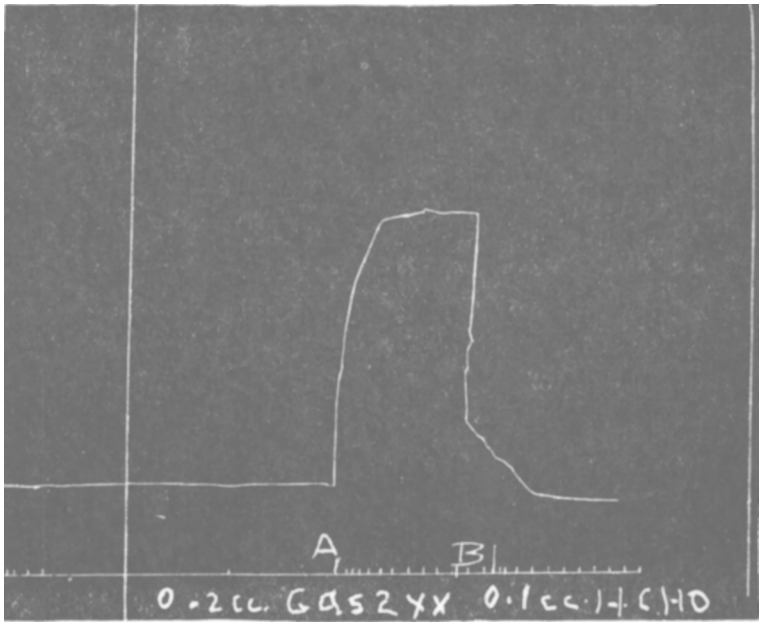
In such a compound, current theory predicates that its physiological activity is intimately associated with the presence of the free aromatic ethylamine group. It follows theoretically that any chemical change involving the elimination of this free NH_2 group from such a compound should reduce, or even destroy the physiological action of the molecule as a whole.

The addition of formaldehyde to primary amines changes them according to the following equation, in accordance with the well known "formol titration" of Henriques and Sörenson:[2]

$$R.CH_2.CH_2.NH_2 + H.CHO = R.CH_2.CH_2.N:CH_2 + H_2O.$$

It has been found by actual experiment that the addition of 0.1 cc. of neutralized formalin solution releases the contracture in a piece of guinea pig intestine which has been induced by either the soluble, physiologically active substance found in cultures of the gas bacillus, or by histamine. The following graph is the record of such a contracture induced by 0.2 cc. of gas bacillus filtrate, and released by 0.1 cc. of formaldehyde solution. Precisely similar ones have been obtained with histamine and formaldehyde.

The formaldehyde-ethylamine compound may be washed out of



the preparation with fresh Tyrode solution, and contracture again induced, indicating that the intestinal muscle is not materially injured by the several reagents.

The experiments seem to indicate that contracture of smooth muscle may be induced by an aromatic ethylamine group, and that chemical change of this ethylamine group may thereby remove the contracture-inducing capacity of the entire molecule.

If 0.2 cc. of formaldehyde solution is added to the Tyrode solution in which the intestinal strip is suspended, and then either gas bacillus filtrate, or histamine be added, no contracture is induced until enough of the latter is present to bind the formaldehyde, with an excess, which then induces contracture. In this regard, the reaction between the ethylamine group and the formaldehyde seems to be fairly quantitative.

[1] Kendall, A. I., and Schmitt, F. O., PROC. SOC. EXP. BIOL. AND MED., 1926, xxiv, 104.

[2] Henriques, V., and Sörensen, S. P. L., *Zeit. f. Physiol. Chem.*, 1909, lx, 1.